

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GROSSET-FOURNIER, Chantal
 Grosset-Fournier & Demachy SARL
 20, rue de Maubeuge
 F-75009 Paris
 FRANCE

Date of mailing (day/month/year) 30 August 2000 (30.08.00)	
Applicant's or agent's file reference WOB 98 BE ID	IMPORTANT NOTIFICATION
International application No. PCT/EP00/00647	International filing date (day/month/year) 27 January 2000 (27.01.00)

1. The following indications appeared on record concerning:

the applicant the inventor the agent the common representative

Name and Address GROSSET-FOURNIER, Chantal Grosset-Fournier & Demachy 20, rue de Maubeuge F-75009 Paris France	State of Nationality	State of Residence
	Telephone No.	
	01 42 81 09 58	
	Facsimile No.	
	01 42 81 08 71	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person the name the address the nationality the residence

Name and Address GROSSET-FOURNIER, Chantal Grosset-Fournier & Demachy SARL 20, rue de Maubeuge F-75009 Paris France	State of Nationality	State of Residence
	Telephone No.	
	01 42 81 09 58	
	Facsimile No.	
	01 42 81 08 71	
	Teleprinter No.	

3. Further observations, if necessary:

The agent's new address on the Demand has been considered as a change under Rule 92bis. In case of disagreement, the International Bureau should be notified immediately.

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer A. Karkachi Telephone No.: (41-22) 338.83.38
Facsimile No.: (41-22) 740.14.35	

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 30 August 2000 (30.08.00)	
International application No. PCT/EP00/00647	Applicant's or agent's file reference WOB 98 BE ID
International filing date (day/month/year) 27 January 2000 (27.01.00)	Priority date (day/month/year) 03 February 1999 (03.02.99)
Applicant KLEIN, Bernard et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

29 June 2000 (29.06.00)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer A. Karkachi Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference WO 98 BE ID	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 00/00647	International filing date (day/month/year) 27/01/2000	(Earliest) Priority Date (day/month/year) 03/02/1999
Applicant I.D.M. IMMUNO-DESIGNED MOLECULES et al		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/00647

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K35/28 A61K35/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 92 21402 A (IMMUNEX CORP) 10 December 1992 (1992-12-10) *cf. abstract, page 6, last para. and page 7, first para., page 8, lines 4-15* ---	1-16
Y	US 5 672 346 A (SROUR EDWARD ET AL) 30 September 1997 (1997-09-30) *cf. abstract* ---	1-16
Y	EP 0 451 611 A (SYSTEMIX INC) 16 October 1991 (1991-10-16) *cf. page 1, lines 9-19, page 3, lines 5-15 ("summary"), page 6, 2nd para., and last line bridging with page 7, first para.* ---	1-16

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
-----------------------------------------------------------	----------------------------------------------------

7 July 2000

14/07/2000

Name and mailing address of the ISA
 European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
 Fax: (+31-70) 340-3016

Authorized officer

Stoltner, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/00647

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 241 578 A (MARROW GROUP INT) 21 October 1987 (1987-10-21) *cf. abstract, and col. 1, lines 25-37* -----	1-16
Y	WO 97 16535 A (SANDOZ LTD ;SYSTEMIX INC (US); SANDOZ AG (DE); SANDOZ AG (AT)) 9 May 1997 (1997-05-09) *cf. page 6, lines 8-12 and 2nd para., page 11, 26-32, page 14, lines 7-16* -----	1-16

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/00647

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9221402	A	10-12-1992		US 5199942 A AU 665955 B AU 2179392 A CA 2109699 A EP 0587754 A JP 6508613 T		06-04-1993 25-01-1996 08-01-1993 10-12-1992 23-03-1994 29-09-1994
US 5672346	A	30-09-1997		AU 4788093 A CA 2141207 A EP 0658114 A WO 9402157 A		14-02-1994 03-02-1994 21-06-1995 03-02-1994
EP 0451611	A	16-10-1991		US 5061620 A AU 641488 B AU 7398691 A CA 2039315 A JP 3017320 B JP 7313150 A JP 2000078968 A US 5914108 A US 5643741 A US 5716827 A US 5750397 A US 5763197 A		29-10-1991 23-09-1993 03-10-1991 01-10-1991 06-03-2000 05-12-1995 21-03-2000 22-06-1999 01-07-1997 10-02-1998 12-05-1998 09-06-1998
EP 0241578	A	21-10-1987		AT 127692 T AU 595813 B AU 5985086 A AU 6815990 A AU 6816090 A AU 615414 B AU 7356887 A BG 51337 A BR 8707673 A CA 1282725 A CA 1310926 A DE 3751519 D DK 665687 A EP 0309456 A FI 884783 A HK 1007684 A HU 48112 A JP 62249926 A JP 10114664 A JP 1503195 T JP 2857392 B KR 142885 B NO 179181 B NZ 218282 A NZ 220038 A RO 106655 A US 4721096 A WO 8706120 A US 5443950 A US 5962325 A US 5460939 A US 5510254 A US 6022743 A		15-09-1995 12-04-1990 22-10-1987 14-03-1991 14-03-1991 03-10-1991 09-11-1987 15-04-1993 15-08-1989 09-04-1991 01-12-1992 19-10-1995 17-12-1987 05-04-1989 17-10-1988 23-04-1999 29-05-1989 30-10-1987 06-05-1998 02-11-1989 17-02-1999 15-07-1998 13-05-1996 28-05-1990 28-08-1990 30-06-1993 26-01-1988 22-10-1987 22-08-1995 05-10-1999 24-10-1995 23-04-1996 08-02-2000

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/00647

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0241578	A	US	5580781 A	03-12-1996
		US	5516680 A	14-05-1996
		US	5512475 A	30-04-1996
		US	5541107 A	30-07-1996
		US	5516681 A	14-05-1996
		US	5578485 A	26-11-1996
		US	5785964 A	28-07-1998
		US	5518915 A	21-05-1996
		US	5624840 A	29-04-1997
		US	5902741 A	11-05-1999
		US	5863531 A	26-01-1999
		US	5266480 A	30-11-1993
		US	5160490 A	03-11-1992
		US	5849588 A	15-12-1998
		US	5858721 A	12-01-1999
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WO 9716535	A	09-05-1997	US 6060052 A	09-05-2000
			AU 717783 B	30-03-2000
			AU 7495396 A	22-05-1997
			CA 2236263 A	09-05-1997
			EP 0858503 A	19-08-1998
			JP 11514879 T	21-12-1999

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WOB 98 BE IDM POI	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP00/00647	International filing date (day/month/year) 27/01/2000	Priority date (day/month/year) 03/02/1999
International Patent Classification (IPC) or national classification and IPC A61K35/28		
<p>Applicant I.D.M. IMMUNO-DESIGNED MOLECULES et al</p> <ol style="list-style-type: none"> This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. This REPORT consists of a total of 7 sheets, including this cover sheet. <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> 		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 		

Date of submission of the demand 29/06/2000	Date of completion of this report 10.05.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Stoltner, A Telephone No. +49 89 2399 8408



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/00647

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-12 as originally filed

Claims, No.:

1-16 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/00647

- the drawings, sheets:
5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- the entire international application.
- claims Nos. 7-12.
- because:
- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. 7-12 (referring to a method of diagnosis).
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP00/00647

Novelty (N)	Yes:	Claims 7
	No:	Claims 1-6, 8-16
Inventive step (IS)	Yes:	Claims 7
	No:	Claims 1-6, 8-16
Industrial applicability (IA)	Yes:	Claims 1-16 (except claims 7-12 referring to a method of diagnosis, with respect to some states within the PCT)
	No:	Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/00647

ad section V:

- 1). The present application concerns cell compositions containing macrophages and their use in cancer immunotherapy and stem cell transplantation.
- D1, WO-A-9 221 402, discloses a method of autologous hematopoietic cell transplantation by a) obtaining hematopoietic cells from bone marrow or peripheral blood, b) expanding said hematopoietic progenitor cells, and c) administering said cellular preparation to the patient (cf. abstract). On page 8, lines 4-15, D1 teaches that the culturing of hematopoietic progenitor cells, in the presence of growth factors, results in the expansion of myeloid and erythroid lineage progenitor cells.
- (D2), US-A-5 672 346, discloses human pluripotent hematopoietic stem cell enriched compositions and their capacity to differentiate into members of erythroid, myeloid and megakaryocytic cell lineages. By grafting human hematopoietic cells in a mammal, peripheral blood cell compositions containing CD14+ cells (macrophages) can be obtained (cf. col. 3, lines 29-35).
- D3, EP-A-451 611, provides human hematopoietic cells (cf. page 3, 2nd para., "Summary of the Invention"). In page 5, last para., a pluripotent human stem cell is defined as giving rise to progeny in all defined hematolymphoid lineage and in their full capacity to reconstitute an immunocompromised human host in all blood cell types and their progenitors. See in this respect also on page 6, lines 5-13 and lines 55-57 on the bottom, where antibodies to CD14+ cells are identified.
- D4, EP-A-241 578, provides a process for replicating bone marrow cells in-vitro including a culture medium with secretory products of extramedullary macrophages (cf. abstract). On col. 1, lines 25-37, the proliferation of a multi potential hematopoietic stem cell with marrow repopulation capability is emphasized.
- D5, WO-A-9 716 535, again stresses the ability of stem cells to proliferate and differentiate into cells of all the hematopoietic lineages (cf. page 6, lines 8-12 and 2nd para.).

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/00647

- 2). Cell compositions containing macrophages are not "expressis-verbis" disclosed in the above cited documents. However, in view that a multi-potential stem cell may develop into cells of all kinds of the hematopoietic and hematolymphoid lineages and in view that in D3 antibodies to CD14+ cells are obtained, the implicit presence of macrophages within cell compositions (including several hematopoietic cell types) has to be derived from the prior art knowledge. The subject-matter of the present claim 1 therefore seems implicitly anticipated with regard to the above cited documents thus failing to comply the requirements set out by Arts. 33(2) and 33(3) PCT.
- 3). A cell composition as depicted in claim 2 is nowhere disclosed nor suggested in the cited prior art documents. Claim 2 as such complies with the requirements of novelty and inventive pursuant to Arts. 33(2) and 33(3) PCT.
- 4). Claims 2-6 and 14-16 are only acceptable if appending to an acceptable preceding claim 1.
- 5). A process for preparing a cell composition as defined in the present claim 7 is nowhere taught nor suggested in the above cited documents. Claim 7 therefore seems to be in line with Arts.33(2) and 33(3) PCT. The same applies to the appending claims 8-13.
- 6). For the assessment of the present claims 7-12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

ad section VIII:

- 1). The back reference of the process claim 11 to the composition claim 6 seems

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/00647

inconsistent and erroneous (Art. 6 PCT).

- 2). The use of the term "about" between ranges should be avoided as its presence may render the scope of protection ambiguous and difficult to distinguish with respect to the prior art teaching.